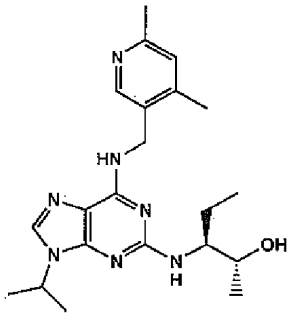
STATEMENT OF INVENTION

Disclosed is a crystalline form of compound (I),

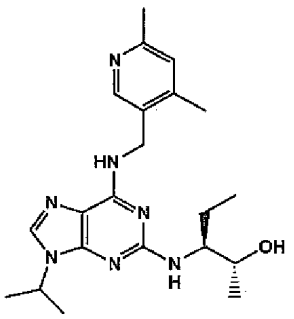


(I)

wherein said compound is in the form of the free base or a pharmaceutically acceptable salt thereof, or a solvated form of the free base or salt form thereof.

The crystalline forms of the disclosure typically demonstrate one or more improved properties over the amorphous form. Suitable properties include, for example, better storage stability, improved ease of handling (flowability, compressibility, stability), easier purification, and easier synthetic scale up

In one aspect, the present invention provides a crystalline form of compound (I),



(I)

wherein said compound is in the form of the free base or a solvate.

Also disclosed is a pharmaceutical composition comprising a crystalline form as described above as an active ingredient and a pharmaceutically acceptable diluent, excipient or carrier.

In another aspect, the present invention provides a pharmaceutical composition comprising the crystalline form disclosed herein and a pharmaceutically acceptable carrier, diluent or excipient

In yet another aspect, the present invention provides a crystalline form as disclosed herein for use in medicine.

Also disclosed is a crystalline form as described above for use in the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

In yet another aspect, the present invention provides an agent for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders, said agent comprising a crystalline form disclosed herein.

In yet another aspect, the present invention providesthe use of a crystalline form disclosed herein in the preparation of a medicament for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders,

neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

Also disclosed is a method for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders, said method comprising administering a pharmacologically effective amount of a crystalline form as described above to a subject in need thereof.

Also disclosed are processes for preparing crystalline forms as described above.

In yet another aspect, the present invention provides a process for preparing crystalline free base (Form A) of compound (I) disclosed herein, said method comprising the steps of crystallising compound (I) in free base Form A from methyl t-butyl ether (MTBE)

DETAILED DESCRIPTION

The crystalline forms of the invention may be characterised by a range of different analytical techniques, including x-ray powder diffraction and differential scanning calorimetry. Further details of these techniques and equipment are set forth in the accompanying examples section.

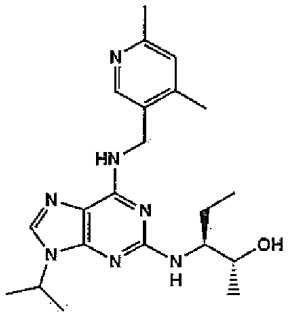
As used herein, the term "solvate" or "solvated form" refers to a crystal having one or more molecules of solvent associated therewith as an inherent part of the crystal structure. Preferably, the solvate or solvated form is the hydrate.

In general, different plural crystalline forms (polymorphs) of the same compound can be produced by varying the crystallisation conditions used. These different crystalline forms have different three-dimensional structures and different physicochemical properties. However, the existence of polymorphs is inherently unpredictable and theoretical calculations to predict polymorphs are extremely unreliable, with many more polymorphs predicted than can actually be isolated in practice.

Preferably, the crystalline forms of the invention are at least 95 % pure (in terms of the purity of the crystal form), more preferably, at least 97 % pure, even more preferably, at least 98 or 99 % pure (for example, as analysed by HPLC). More preferably still, the crystalline forms of the invention are at least 99.5 % pure.

CLAIMS

1. A crystalline form of compound (I),



(I)

wherein said compound is in the form of the free base or a solvate.

2. A crystalline form according to claim 1, which is characterized by an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 9.60 ± 0.2, 10.22 ± 0.2, 11.29 ± 0.2, 11.66 ± 0.2, 12.26 ± 0.2, 12.62 ± 0.2, 13.17 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2, 15.15 ± 0.2, 15.57 ± 0.2, 16.99 ± 0.2, 17.68 ± 0.2, 18.30 ± 0.2, 18.39 ± 0.2, 18.63 ± 0.2, 18.97 ± 0.2, 19.32 ± 0.2 and 20.20 ± 0.2 [Form A].

3. A crystalline form according to claim 2 wherein the x-ray powder diffraction pattern comprises two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 12.26 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2 and 15.57 ± 0.2.

4. A crystalline form according to any preceding claim, which is characterized by an x-ray powder diffraction pattern in which the peak positions are substantially in accordance with the peak positions of the pattern shown in Figure 5 or listed in Table 1.

5. A crystalline form according to any preceding claim, which is characterized by a differential scanning calorimetry trace recorded at a heating rate of 20°C per minute which shows a maximum endothermic peak at a temperature between about 130°C and about 140°C.

6. A crystalline form according to any preceding claim, which is characterized by a differential scanning calorimetry trace substantially in accordance with that shown in Figure 6.

7. A crystalline form according to any preceding claim, which is monoclinic P21/c space group with unit cell dimensions of a = 15.19 ± 2 Å, b = 18.34 ± 2 Å, c = 8.65 ± 2 Å and [beta] = 95.53 ± 2°.

8. A pharmaceutical composition comprising the crystalline form according to any one of claims 1 to 7 and a pharmaceutically acceptable carrier, diluent or excipient.

9. A crystalline form according to any one of claims 1 to 7 for use in medicine.

10. An agent for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders, said agent comprising a crystalline form according to any one of claims 1 to 7.

11. The use of a crystalline form according to any one of claims 1 to 7 in the preparation of a medicament for the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

12. A process for preparing crystalline free base (Form A) of compound (I) according to claim 1, said method comprising the steps of crystallising compound (I) in free base Form A from methyl t-butyl ether (MTBE).